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TITLE: New nucleic acid constructs useful for transforming cells useful as a drug delivery vehicle

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ABSTRACTED-PUB-NO: WO 200136643A

BASIC-ABSTRACT: NOVELTY - Nucleic acid constructs (N1) for expression of a small peptide is new.

DETAILED DESCRIPTION - (N1) comprises:

(1) a nucleic acid sequence encoding a signal peptide;

(2) a nucleic acid sequence which encodes the pro-region of a somatostatin or a functional fragment or analog of it; and

(3) a nucleic acid encoding a small peptide.

A significant "fragment" in a nucleic acid context is a contiguous segment of at least about 17 nucleotides, generally at least 20 nucleotides, more generally at least 23 nucleotides, ordinarily at least 26 nucleotides, more ordinarily at least 29 nucleotides, often at least 32 nucleotides, more often at least 35 nucleotides, typically at least 38 nucleotides, more typically at least 41 nucleotides, usually at least 44 nucleotides, more usually at least 47 nucleotides, preferably at least 50 nucleotides, more preferably at least 53 nucleotides, and in particularly preferred embodiments will be at least 56 or more nucleotides. Said fragments may have termini at any location, but especially at boundaries between structural domains.

In other embodiments, the invention provides polynucleotides (or polypeptides) which comprise a plurality of distinct, e.g., nonoverlapping, segments of the specified length. Typically, the plurality will be at least two, more usually at least three, and preferably 5, 7, or even more. While the length minima are provided, longer lengths, of various sizes, may be appropriate, e.g., one of length 7, and two of length 12.

A DNA which codes for an IL-170 protein will be particularly useful to identify genes, mRNA, and cDNA species which code for related or homologous proteins, as well as DNAs which code for homologous proteins from different species. There are likely homologues in other species, including primates. Various CTLA-8 proteins should be homologous and are encompassed herein. However, even proteins that have a more distant evolutionary relationship to the antigen can readily be isolated under appropriate conditions using these sequences if they are sufficiently homologous. Primate CTLA-8 protein proteins are of particular interest.

This invention further covers recombinant DNA molecules and fragments having a DNA sequence identical to or highly homologous to the isolated DNAs set forth herein. In particular, the sequences will often be operably linked to DNA segments which control transcription, translation, and DNA

INDEPENDENT CLAIMS are included for:

(1) a cell (I) comprising:

(a) an exogenous nucleic acid sequence which comprises a nucleic acid sequence encoding a signal peptide and a nucleic acid sequence which encodes the pro-region of a somatostatin or a functional fragment or analog of it; and

(b) a nucleic acid sequence encoding a small peptide, where the cell is capable of expressing the small peptide;

(2) making (M1) a small peptide comprising culturing (I);

(3) making (M2) a cell capable of expressing a small peptide comprising:

(a) providing a cell; and

(b) introducing (N1) into the cell;

(4) making (M3) a cell capable of expressing a small peptide comprising:

(a) providing a cell; and

(b) introducing into the genome of the cell an exogenous nucleic acid sequence which comprises the pro-region of a somatostatin linked to a nucleic acid sequence within the genome of the cell which encodes a small peptide;

(5) treating (M4) a subject comprising administering to the subject an exogenous nucleic acid sequence comprising:

(a) a nucleic acid sequence encoding a signal peptide;

(b) a nucleic acid sequence which encodes the pro-region of a somatostatin or a functional fragment of it; and

(c) a nucleic acid sequence encoding a small peptide, such that the small peptide is expressed; and

(6) treating (M5) a subject comprising administering (I) to the subject.

ACTIVITY - None given.

MECHANISM OF ACTION - Gene therapy.

USE - Transfected primary or secondary cells or cell strains have wide applicability as a vehicle or delivery system for therapeutic proteins.

ADVANTAGE - An advantage of the use of transfected or secondary cells is that by controlling the number of cells introduced into an individual, one can control the amount of the protein delivered to the body. In addition, in some cases, it is possible to remove the transfected cells of there is no longer a need for the product. A further advantage of treatment by use of tranfected primary or secondary cells of the present invention is that production of the therapeutic product can be regulated, such as through the an administration of zinc, steroids or an agent which affects transcription of a protein, product, or nucleic acid product or affects the stability of a nucleic acid product.

CHOSEN-DRAWING: Dwg.0/7

TITLE-TERMS:
NEW NUCLEIC ACID CONSTRUCTION USEFUL TRANSFORM CELL USEFUL DRUG DELIVER VEHICLE

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replication. Alternatively, recombinant clones derived from the genomic sequences, e.g., containing introns, will be useful for transgenic studies, including, e.g., transgenic cells and organisms, and for gene therapy. See, e.g., Goodnow (1992) "Transgenic Animals" in Roitt (ed.) Encyclopedia of Immunology Academic Press, San Diego, pp. 1502-1504; Travis (1992) Science 256:1392-1394; Kuhn, et al. (1991) Science 254:707-710; Capecchi (1989) Science 244:1288; Robertson (ed. 1987) Teratocarcinomas and Embryonic Stem Cells: A Practical Approach IRL Press, Oxford; Rosenberg (1992) J. Clinical Oncology 10:180-199; and Cournoyer and Caskey (1993) Ann. Rev. Immunol. 11:297-329.

Homologous nucleic acid sequences, when compared, exhibit significant similarity. The standards for homology in nucleic acids are either measures for homology generally used in the art by sequence comparison or based upon hybridization conditions. The hybridization conditions are described in greater detail below.

Substantial homology in the nucleic acid sequence comparison context means either that the segments, or their complementary strands, when compared, are identical when optimally aligned, with appropriate nucleotide insertions or deletions, in at least about 50% of the nucleotides, generally at least 56%, more generally at least 59%, ordinarily at least 62%, more ordinarily at least 65%, often at least 68%, more often at least 71%, typically at least 74%, more typically at least 77%, usually at least 80%, more usually at least about 85%, preferably at least about 90%, more preferably at least about 95 to 98% or more, and in particular embodiments, as high at about 99% or more of the nucleotides. Alternatively, substantial homology exists when the segments will hybridize under selective hybridization conditions, to a strand, or its complement, typically using a sequence derived from Table 1, 2, or 3. Typically, selective hybridization will occur when there is at least about 55% homology over a stretch of at least about 14 nucleotides, preferably at least about 65%, more preferably at least about 75%, and most preferably at